REMARKS

Applicants acknowledge receipt of the Office Action mailed on May 1, 2003 (Paper No. 8). Claims 1-9 are pending in the application. The PTO has maintained its previous rejections of Claims 1-2 and 7-8 under 35 U.S.C. §102(e) as being anticipated by Carthron (U.S. Patent No. 6,277,842). The previous rejections of Claim 1-4 and 6-9 under 35 U.S.C. §102(e), as being anticipated by Carthron (U.S. Patent No. 6,277,842), have also been maintained. The rejection of Claims 1-9 under 35 U.S.C. §103(a), as being obvious in view of Carthron and De La Harpe et al. (U.S. Patent No. 5,980,905), were likewise maintained.

Claims 1 and 8 have been amended in order to clarify the purposes for the compositions recited by those claims in response to an Examiner suggestion. Support for the amendments to Claims 1 and 8 can be found throughout the specification and in the original claims as filed. Claims 1-9 are presented for examination. Reconsideration and withdrawal of the present rejections in view of the comments presented herein are respectfully requested.

Claims 1-2 and 7-8 are not anticipated

The PTO previously rejected Claims 1-2 and 7-8 under 35 U.S.C. §102(e) as being anticipated by Carthron (U.S. Patent No. 6,277,842). In the previous Office Action (paper no. 5), the Examiner alleged that the compositions of Carthron anticipate those of the Instant claims because the compositions contain chromium picolinate and alpha lipoic acid. Applicants argued in the response to the previous Office Action that the Claims 1-2 and 7-8 are not anticipated by Carthron because the claims of Carthron do not teach each and every limitation of the Instant claims. Specifically, the compositions of Carthron contain multiple pharmacologically active ingredients, whereas the compositions of the Instant claims consist essentially of a chromium complex and alpha lipoic acid. The Examiner found the argument unpersuasive in the present Office Action and the rejection of Claims 1-2 and 7-8 under 35 U.S.C. §102(e) as being anticipated by Carthron was maintained.

Under 35 U.S.C. §102(e), "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference". *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ 1051, 1053 (Fed. Cir. 1987). M.P.E.P. §2131. The instant claims read on compositions consisting

essentially of a chromium complex and alpha lipoic acid. In order for a prior art reference to anticipate the instant claims, the reference must contain, or expressly or inherently describe, a composition consisting essentially of a chromium complex and alpha lipoic acid.

In the present Office Action, the Examiner has indicated that the term 'consisting essentially of' limits the scope of a claim by excluding additional materials or steps that materially affect the basic and novel characteristics of the invention. The pending composition claims do not list an intended purpose for the composition. The Examiner contends that the relevant question is whether "the additional ingredients actually effect the basic and novel characteristics of the invention" (page 3 of paper 8).

The claims have now been amended to include a purpose for the claimed compositions. Claims 1 and 8 are now directed toward compositions for improving insulin sensitivity. Support for this amendment to the claims can be found in the Summary of the Invention and Detailed Description sections. With the addition of a purpose for the claimed composition, the basic and novel characteristics of the invention have been clarified. The improvement in insulin sensitivity stems from the effect that the ingredients of the claimed compositions, a chromium complex and alpha lipoic acid, have on the uptake of glucose at a cellular level. The compositions of the present invention act on a cellular level to synergistically increase the uptake of glucose. As demonstrated in Example 1 of the specification, the two components of the claimed compositions, chromium and alpha lipoic acid, act synergistically to increase the uptake of glucose by skeletal muscle cells *in vitro*. It is this effect on glucose uptake at the cellular level that creates the benefits to the individual consuming the compositions of the invention.

The Examiner has rejected Claims 1-2 and 7-8 under 35 U.S.C. §102(e) as being anticipated by Carthron (U.S. Patent No. 6,277,842). In the current Office Action, referring to the ingredients of the composition disclosed in Carthron, the Examiner has asked if the additional ingredients would actually effect the basic and novel characteristics of the invention. With the clarification of the basic and novel characteristics of the invention created by the addition of a purpose for the claimed compositions, Applicants argue that the additional ingredients of Carthron would indeed alter the basic and novel characteristics of the invention.

The compositions of Carthron include ingredients which would alter the uptake of glucose on a cellular level. For example, one ingredient, L-carnitine, has been shown by

researchers to significantly increase blood glucose uptake in patients receiving the compound versus patients receiving a placebo (Giancaterini, A. (2000) *Metabolism* **49**:704-708). In this study, researchers found that the reduction in blood glucose was due to increases in cellular glucose storage and not due to an increase in the metabolism of glucose. Thus, the addition of L-carnitine to the claimed compositions of the present invention would clearly have an effect on the basic and novel characteristics of the invention, those characteristics being due to the effects of chromium and alpha lipoic acid on glucose uptake at a cellular level. An ingredient like L-carnitine is expressly excluded from the Instant claims by use of the phrase 'consisting essentially of', which limits the scope of a claim by excluding additional materials or steps that materially affect the basic and novel characteristics of the invention. Since the methods of Carthron describe the use of ingredients that would materially affect the basic and novel characteristics of the present invention if they were added to the claimed compositions of the present invention, these methods do not anticipate the Instant claims.

In a related issue, the Examiner claims that the incorporation of nicotinic acid into the composition of the invention as a chelating agent confuses the meaning of the term 'consisting essentially of'. The Examiner argues that the claims envision the inclusion of nicotinic acid in compositions 'consisting essentially of' a chromium complex and alpha lipoic acid. The Examiner questions how the term 'consisting essentially of' can exclude the ingredients of Carthron while simultaneously permitting the inclusion of nicotinic acid, with its positive effect of the activity of the composition.

The PTO has overlooked the form of the claims. The claims that recite three essential ingredients, including the chelating agent, Claims 8 and 9, are a completely separate group of claims from those that recite only two essential ingredients. Because the chelating agent alters the absorption of chromium, Applicants have treated that as a different combination. Note that Claim 8 is a separate independent claim. It is not dependent on Claim 1. Thus, there is no inconsistency or confusion in either claim set. In each case, the independent claims recite the ingredients that define the essential activities in the combination.

With respect to the heart of the anticipation rejection, the PTO seems to take the position that the additional ingredients of Carthron would not effect the basic and novel characteristics of the invention. The Examiner also states that if an applicant contends that additional steps or

materials in the prior art are excluded by the recitation of "consisting essentially of", the applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. This burden has clearly been satisfied here. In the study noted above, L-carnitine supplementation was shown to have significant effects on blood glucose levels and glucose storage. Thus, it seems beyond question that the claimed method of Carthron contains additional ingredients beyond chromium and alpha lipoic acid, and that these added ingredients alter the characteristics of the composition relating to glucose uptake and processing.

In consideration of the arguments and evidence presented above, it is clear that U.S. Patent No. 6,277,842, to Carthron, does not anticipate Claim 1-2 and 7-8 under 35 U.S.C. §102(e).

Claims 1-9 are not obvious

In the previous Office Action, the Examiner rejected Claims 1-4 and 6-9 under 35 U.S.C. §103(a) as being obvious in light of the Carthron patent (U.S. Patent No. 6,277,842).

The Examiner also rejected Claims 1-9 under 35 U.S.C. §103(a) as being unpatentable over Carthron in view of De La Harpe et al. (U.S. Patent No. 5,980,905). De La Harpe et al. teaches a composition containing chromium and chelating agents, coated onto microbeads and optionally enterically coated. The Examiner asserted that this disclosure, along with the disclosure of Carthron, would motivated one with skill in the art to coat the composition of Carthron onto microbeads as taught by De La Harpe et al.

The Examiner has stated that the continued rejection of the claims stems in part from a lack of substantial evidence present by the Applicants that shows that the other ingredients of Carthron would have an effect on the basic and novel characteristics of the Invention. However, the added ingredients clearly have pharmacological activity. Indeed, the effects that the other ingredients have on glucose metabolism and the resulting effects on insulin sensitivity, hyperglycemia, and hypercholesterolemia are readily available in medical and scientific research literature. For example, as discussed above on page 5, Giancaterini et al. have found that supplementation with L-carnitine by itself significantly increases blood glucose uptake by stimulating the storage of glucose in cells. As seen in the data from Example 1 of the instant

specification, different agents that individually affect a certain function or property can have unpredictable additional or synergistic effects when given in conjunction with each other. Thus, it would be reasonable to assume that the inclusion of L-carnitine in a composition that consists essentially of alpha lipoic acid and a chromium complex would influence the activity of the composition, but what that effect or influence would be is unknowable without substantial experimentation.

Other ingredients in the composition of Carthron have also been demonstrated to affect glucose metabolism and other pharmacological properties. Supplementation with creatine has been found to increase fasting blood glucose levels and increase the response of blood glucose levels to a glucose load while not affecting the response of blood glucose levels to insulin release (Rooney et al. (2003) *Ann Nutr Metab* **47**:11-15). In studies of the effects of high-dose niacin treatment on the blood lipid profiles of hypertriglyceridaemic patients, researchers found that blood glucose levels increased by 13% while intravenous glucose tolerance decreased by 26% after niacin treatment (Walberg et al. (1992) *Scand J Clin Nutr* **52**:537-545). These reports illustrate the profound effects that the ingredients of Carthron's method can have on glucose metabolism. These effects would impact the basic and novel characteristics of the invention and thus are excluded by the term 'consisting essentially of' in the Instant claims.

The Examiner asserts that the motivation to combine the references can be obtained solely on the basis of the disclosures of the references. However, there is no teaching or suggestion in the references to eliminate the other active ingredients. Nowhere in any of the cited references is there any suggestions that a composition *consisting essentially of* alpha lipoic acid and a chromium complex, without any of the other featured ingredients of Carthron's method, would be advantageous to give to a patient, in order to provide any benefits other than those already attributed to the separate and distinct functions of alpha lipoic acid and chromium individually. The Instant specification provides evidence of a synergistic effect on glucose uptake with the concurrent administration of alpha lipoic acid and a chromium complex, which is a novel and unpredictable discovery that a composition with only these two ingredients will have a surprising effect. With no previous evidence in existence that such an effect would occur with administration of this composition, no previous motivation for creating such a composition could have existed.

Applicants assert that the disclosures of the two cited references do not provide the basic criteria for a *prima facie* case of obviousness. The references do not contain any information that would lead one with skill in the art to believe that there would be any advantageous properties to a composition consisting essentially of alpha lipoic acid and a chromium complex , lacking all of the other key ingredients included in the methods of Carthron. Thus, there is no motivation in the references to modify the methods of Carthron to create a composition. The disclosure of the beneficial properties of alpha lipoic acid administration and of the beneficial properties of chromium administration, discussed separately in Carthron, do not provide motivation to create a composition consisting essentially of the two compounds for the synergistic upregulation of glucose uptake on a cellular level. Thus, a person with ordinary skill in the art at the time of Invention, given the disclosures of Carthron and De La Harpe et al., would have had no reason to create a composition consisting essentially of alpha lipoic acid and chromium without the other ingredients listed by Carthron. In light of the disclosures of the cited references, had a person with ordinary skill in the art created such a composition, for whatever reason, that person would have had no reasonable expectation of seeing any effect upon administration of the composition other than an additive effect created by the temporal combination of the individual, separate effects of alpha lipoic acid administration and chromium administration. The references do not teach all of the limitations of the present claims, since the compositions disclosed by the references either lack key ingredients of the compositions of the Invention, or contain additional ingredients shown in the literature to have profound effects on glucose metabolism and thus are excluded from the present claims with the inclusion of the phrase 'consisting essentially of'. Because the cited references do not provide motivation to combine or modify their disclosure, do not provide a reasonable expectation of success should the disclosures be combined or modified, and do not teach all of the limitations of the Instant claims, the cited references fail to provide any of the basic criteria for a *prima facie* case of obviousness.

Even if there were a *prima facie* case of obviousness, in which it could be shown that there is some suggestion to eliminate all the other active ingredients and focus in on this one combination, the evidence of synergy overcomes any such *prima facie* case.

In view of the deficiencies discussed above, the Carthron and De La Harpe et al. references, separately or in combination, are not sufficient to support a *prima facie* case of obviousness. Therefore, Applicants request withdrawal of these rejections.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the present application is in condition for allowance. Nevertheless, the PTO is invited to contact the undersigned at the telephone number appearing below to discuss any remaining issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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